

Assessing Acrylamide Cancer Potency, Including Bioavailability and Sensitive Populations

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New Studies Are Needed to Determine Whether Acrylamide in Food Poses a Risk to Human Health

- The new research data showing the large number of foods containing acrylamide present in the human diet makes continued application of the current NSRL of $0.2\mu\text{g}/\text{day}$ problematic
- A variety of studies are needed to assess the risk, if any, posed by acrylamide in food
- Such studies include:
 - Bioavailability studies
 - Biomarker studies
 - Metabolic and toxicokinetic studies

Bioavailability Studies Will Assist In Human Risk Assessment

- A fundamental consideration in human risk assessment is the bioavailability of the chemical of interest
 - The route of exposure can affect bioavailability
- Past studies considered the ingestion of acrylamide – a highly water soluble molecule – via drinking water
- Bioavailability of acrylamide in food is currently unclear as there has been no past work on food as a route of exposure

Biomarker Studies Also Will Assist In Human Risk Assessment

➤ Biomarkers of Exposure:

- Indicates exposure to a substance over time
- Acrylamide hemoglobin adduct studies have been done on rodents
- Swedes have done acrylamide hemoglobin adduct studies on smokers and exposed workers
- Other studies are on-going

➤ Biomarkers of Effect:

- Indicates biological effect of substance exposure
- Studies focus on target organs to determine cellular and DNA damage
- No past work was done relating to acrylamide exposure from foods

Metabolic & Toxicokinetic Studies Also Will Assist in Human Risk Assessment

- Metabolic activation:
 - Studies have shown that acrylamide is metabolized into glycidamide
 - This is the probable metabolic pathway for carcinogenic effects of acrylamide
- Major detoxification pathway for acrylamide:
 - Glutathione pathway leading to enhanced excretion of acrylamide
 - Research Triangle Institute is currently conducting a human study with labeled acrylamide
- These studies will be used to improve PBPK model in rodents and enhance interpretation of rodent studies to more accurately assess human risk

Future Work Will Clarify Human Risk Assessment Issues

- Bioavailability: National Center for Toxicological Research (NCTR) will conduct studies on bioavailability in feed for rodents
- NCTR work will be used in planned National Toxicology Program (NTP) rodent feeding studies that are part of FDA's Action Plan
- NCTR bioavailability work also will allow better correlation between planned rodent study results and impact of acrylamide in food on humans

Future Work Will Clarify Human Risk Assessment Issues

➤ Biomarkers:

- FDA Action Plan calls for working with the CDC to use National Health and Nutrition Examination Survey (NHANES) database to correlate the adduct data from rats with adduct measurements in humans
 - This is a significant aspect of the FDA Action Plan as it involves human study
- CDC is collaborating with the FDA to conduct a study of how acrylamide and glycidamide hemoglobin adduct concentrations in volunteer subjects change over several weeks with defined changes in specific food sources of acrylamide in the diet
- NCTR rodent feeding studies will include ancillary studies on biomarkers that will allow better correlation between planned rodent study results and impact of acrylamide in food on humans

➤ Metabolic Studies:

- NCTR will study both acrylamide and glycidamide in studies ancillary to the planned two-year rodent feeding studies